Although circumstantial evidence shows that treatment with metformin may be linked with lactic acidosis, no causal relation has been proved. Metformin is proved to reduce plasma glucose and complications of diabetes. Uniquely, it is the only hypoglycaemic agent to date that has been shown to reduce the macrovascular complications of diabetes.[1] Current published guidelines vary and may limit the use of metformin and cause confusion among doctors. It is essential that the benefits of treatment with metformin be made available to as wide a group of appropriate patients as possible without laying prescribers open to criticism or litigation in the event of concomitant lactic acidosis. A simplified and pragmatic set of guidelines should be adopted, stressing the importance of renal clearance of metformin and withdrawal of metformin in patients with tissue hypoxia.

As metformin is the only oral hypoglycaemic agent proved to reduce cardiovascular mortality, its use should be as widespread as possible in type 2 diabetes. We hope that these suggested guidelines are less ambiguous than current ones and prevent the current situation of many clinicians, who are having to ignore written contraindications in order to maximise the use of metformin appropriately.

G C Jones *consultant physician*
(greg.jones@northglasgow.scot.nhs.uk)

J P Macklin *senior house officer*

Department of Diabetes, Gartnavel General Hospital, Glasgow G12 0YN

W D Alexander *consultant physician*

Diabetes Centre, Western General Hospital, Edinburgh EH4 2XU

Competing interests: None declared.

1 UK Prospective Diabetes Study Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 1998;352:854-65.
2 Brown JB, Pedula, MS, Barzilay J, Herson MK, Latare P. Lactic acidosis rates in type 2 diabetes. *Diabetes Care* 1998;21:1659-63.
3 Cusi K, Consoli A, DeFronzo RA. Metabolic effects of metformin on glucose and lactate metabolism in non insulin-dependent diabetes mellitus. *J Clin Endocrinol Metabol* 1996;81:4059-67.
4 Scheen AJ. Clinical pharmacokinetics of metformin. *Clin Pharmacokinet* 1996;30:359-71.
5 Lalau JD, Lacroix C, De Cagny B, Fournier A. Metformin associated lactic acidosis in diabetic patients with acute renal failure. A critical analysis of its pathogenesis and prognosis. *Nephrol Dial Transplant* 1994;9:126-9.
6 Lalau JD, Race JM. Lactic acidosis in metformin therapy: searching for a link with metformin in reports of "metformin associated lactic acidosis". *Diabetes Obes Metabol* 2001;3:195-201.
7 Misbin RI, Green L, Stadel BV, Gueriguian JL, Gubbi A, Fleming GA. Lactic acidosis in patients with diabetes treated with metformin. *N Engl J Med* 1998;338:265-6.
8 Salpeter S, Greyber E, Pasternak G, Salpeter E. Risk of nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2002;(2):CD002967.
9 Malmberg K, for the Diabetes Mellitus Insulin Glucose Infusion in Acute Myocardial Infarction (DIGAMI) Study Group. Prospective randomised study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. *BMJ* 1997;314:1512-5.
10 Hart SP, Walker JD. Is metformin contra-indicated in diabetic patients with chronic stable heart failure? *Pract Diabetes Int* 1996;13:18-20.
11 Sulkin TV, Bosman D, Krentz AJ. Contraindications to metformin therapy in patients with NIDDM. *Diabetes Care* 1997;20:925-8.
12 Emslie-Smith AM, Boyle DIR, Evans JMM, Sullivan F, Morris AD. Contraindications to metformin therapy in patients with type 2 diabetes—a population-based study of adherence to prescribing guidelines. *Diabet Med* 2001;18:483-8.

Evidence based policy making

Impact on health inequalities still needs to be assessed

Powerful, rich, and well educated people tend to live longer and healthier lives than their less advantaged counterparts. These socioeconomic inequalities in health have been observed in a range of societies—developed, developing, market led, welfare state, and communist. Their expression, however, may vary according to how the particular society is stratified—for example, by income or wealth in the United States, by social class in the United Kingdom, or by education in Europe. They occur across a wide range of causes of death and types of illness, have been observed since accurate statistics were first available, and seem to have been increasing.[1]

Several governments have recently proposed strategies to reduce socioeconomic inequalities in health.[2–5] An issue rendering strategy development in this field difficult is that, although a lot of information is available about the magnitude and causes of socioeconomic inequalities in health, rather less information is available about the effectiveness of policies in reducing them.[6] The recent Cross-Cutting review in England noted that intervention research is scanty compared with the much larger body of observational evidence that describes inequalities.[5] This is shown by the fact that the review contains six boxed lists, containing between them 50 examples of inequalities in health and only one box with rather general, and mainly process related, recommendations for successful interventions.[5]

Unfortunately, knowing the prevalence and causes of a health problem does not always tell us the most effective way to reduce it. For example, knowing the links between smoking and lung cancer, child labour and poor health, or HIV and AIDS may help provide goals such as reducing smoking, child labour, or risky sex, but does not necessarily tell us how to achieve these goals. As is apparent from several fields, the plausibility of proposed interventions is no guarantee of their actual efficacy.[7] Thus anyone wanting to reduce inequalities in health is faced with a lack of information about what actions would be most successful.

Why do we lack this information? Firstly, many studies, such as a recent randomised controlled trial of supplementation with antioxidant vitamin to prevent heart disease and cancer,[8] do not report whether

BMJ 2003;326:5–6

differential effects by social class were observed. One might predict that disadvantaged people with diets below some threshold of adequacy could have benefited, but such studies may not have the power to examine the existence of such differential effects. Conversely, interventions with overall health benefits might result in persisting or widening inequalities (as has been reported for immunisation uptake in the north of England[9] and use of folic acid before conception in the Netherlands.[10] Most studies, including systematic reviews, simply do not report whether any socioeconomic differences in effectiveness have been noted.

Secondly, in the United Kingdom at least, public health research often focuses more on documenting problems and describing the process of trying to solve them than on evaluating the effectiveness of proposed solutions. A recent review for the Health Development Agency found that only 4% of public health research in the United Kingdom dealt with interventions, rather than descriptions of problems, and of this proportion, only 10% (0.4% of the total) focused on the outcomes of the interventions.[11]

Thirdly, asking for higher standards of evidence of the effectiveness of interventions is sometimes deemed to be a recipe for inaction, and doing something is felt to be better than doing nothing.[12] However, these "somethings" should, as the Acheson committee recommended and the United Kingdom's government agreed, be monitored for their impact on inequalities in health.[2] Although reducing such inequalities in health has been an overarching goal of public health policy over the past five or so years in the United Kingdom, initiatives aiming to do this have often been set up in ways that make it difficult to estimate their overall effects or impact on inequalities.

Programmes such as health action zones in England and health demonstration projects in Scotland are being evaluated, but many such initiatives are not designed to facilitate robust evaluation of outcomes. The random allocation of individuals or communities to receive new programmes is often regarded as unacceptable (for example, random allocation of communities to the "Sure Start" programme was ruled out at ministerial level). But when scarce resources can be directed only towards a limited set of places or people, why not randomise those who do or do not receive them, or phase their introduction, to allow systematic evaluation of their effects? For example, if funds are available for only 10 health action zones,[13] and who gets them depends partly on the advocacy skills of local residents, perhaps it would be fairer, as well as more informative, not to choose the 10 poorest or most vociferous areas but the poorest 20, then randomise them to intervention and comparison arms and monitor the impact.

Fourthly, although the British government endorsed the principle of assessing the impact of inequalities in health, this has increasingly become interpreted as a screening and scoping activity (trying to anticipate what impact a proposed programme might have on inequalities) rather than as a monitoring activity (assessing what impact the programme has actually had).[14] Unless we undertake the monitoring task, however, we will not have the information on which to base the predictive exercise.

If governments are serious about wanting to reduce inequalities in health they should not necessarily wait until we have better evidence about the relative effectiveness of different strategies. They should encourage the systematic collation and dissemination of the best international evidence of effectiveness, as has been done in Sweden and the Netherlands,[3 4] and is being done in the United Kingdom through the Health Development Agency's "Evidence into Practice" programme.[15] They should encourage research studies and routine statistics to be designed so that differential effects on, or trends among, different socioeconomic groups can be detected. Most importantly, they should design and implement social and public health initiatives in ways which facilitate good quality evaluations of effectiveness and monitoring of impact on health inequalities.

Sally Macintyre *Director*

Medical Research Council Social and Public Health Sciences Unit, Glasgow G12 8RZ (sally@msoc.mrc.gla.ac.uk)

Competing interests: None declared.

1 Macintyre S. The Black report and beyond; what are the issues? *Soc Sci Med* 1997;44:723-46.
2 Acheson D. *Independent inquiry into inequalities in health: report*. London: Stationery Office, 1998.
3 Swedish National Committee for Public Health. Health on equal terms: national goals for public health. *Scand J Public Health* 2001;29(suppl 57):1-68.
4 Mackenbach J, Stronks K. A strategy for tackling health inequalities in the Netherlands. *BMJ* 2002;325:1029-32.
5 HM Treasury, Department of Health. *Tackling health inequalities: 2002 Cross-Cutting Review*. London: Stationery Office, 2002.
6 Macintyre S, Chalmers I, Horton R, Smith R. Using evidence to inform health policy: case study. *BMJ* 2001;322:222-5.
7 Macintyre S, Petticrew M. Good intentions and received wisdom are not enough. *J Epidemiol Community Health* 2000;54:802-3.
8 Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:23-33.
9 Reading R, Colver A, Openshaw S, Jarvis S. Do interventions that improve immunisation uptake also reduce social inequalities in uptake? *BMJ* 1994;308:1142-4.
10 de Walle H, van der Pal K, de Jong-van den Berg L, Jeeninga W, Schouten J, de Rover C, et al. Effect of mass media campaign to reduce socioeconomic differences in women's awareness and behaviour concerning use of folic acid: cross sectional study. *BMJ* 1999;319:291-2.
11 Milward L, Kelly M, Nutbeam D. Public health intervention research: the evidence. London: Health Development Agency, 2001.
12 Davey Smith G, Ebrahim S, Frankel S. How policy informs the evidence. *BMJ* 2001;322:184-5.
13 Jacobson B, Yen L. Health action zones. *BMJ* 1998;316:164.
14 European Centre for Health Policy. Health impact assessment: main concepts and suggested approach (Gothenburg consensus paper). Brussels: World Health Organization Regional Office for Europe, 1999.
15 NHS Health Development Agency. Search for evidence. London: HDA, 2002. http://194.83.94.80/hda/docs/evidence/eb2000/corehtml/search.jsp (accessed 6 Dec 2002).